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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/822,080	03/30/2001	C. Neal Stewart	19603/2420 (CRF D-2354)	8901

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EXAMINER

IBRAHIM, MEDINA AHMED

ART UNIT PAPER NUMBER

1638

DATE MAILED: 03/27/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/822,080

Applicant(s)

STEWART ET AL.

Examiner

Medina A Ibrahim

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 January 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) 14-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 March 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in Paper No. 12 is acknowledged. The traversal is on the ground(s) that the three groups of invention as set forth in the last Office action are closely related and would require common areas of search and consideration. Therefore, Applicant's urge, the restriction requirement between Groups I, II, and III should be withdrawn. Applicant's argument has been fully considered and is found persuasive only with respect to the restriction between Groups I and II.

Applicant's argument regarding the restriction requirement between Groups I and Group III is not persuasive because the method of Group III requires application of a serine proteinase inhibitor to the plant/ seed which is not required by the invention of Group I, while the invention of Group I requires a DNA and transformation of the plant with the DNA which are not required by the invention of Group III. Therefore, Groups I and III would require different areas of search and consideration, and their coexamination will pose serious burden upon the Examiner. Therefore, the requirement is still deemed proper and is therefore made FINAL.

Claims 1-28 are pending.

Claims 1-20 are under examination.

Claims 21-28 are withdrawn from consideration as being drawn to a non-elected invention.

Sequence Listing

Applicant's CRF and paper sequence listing have been entered.

Drawings

The drawings filed with this application are approved by the Examiner.

Objections

In claim 1, "an operatively linked to a heterologous DNA" should be ---an operably linked heterologous DNA---.

Claims 2, 9 and 12, are objected to because the claims recite more than one period. It is suggested that "SEQ. ID. NO." is changed to ---SEQ ID NO:---. Also, "an amino acid sequence of SEQ. ID. NO. 2" and "a nucleotide sequence of SEQ. ID. NO. 1" lack proper article. It is suggested that "an" be replaced with ---the---. Also, "hybridizes at to" should be changed to ---hybridizes to---.

In claims 9-13 and 15-20, "A" should be replaced with ---The---.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, it is unclear whether "having antibiosis activity" refers to the inhibitor. If so, it is unclear how serine proteinase inhibitors having antibiosis activity would be different from those without antibiosis activity. Dependent claims 2-13 are included in the rejection.

Claims 2, 9 and 12 are indefinite because the hybridization conditions are unclear because time or duration of the hybridization in the buffer is not specified.

In claim 4, "transduced" should be changed to ---transformed---, for clarification.

In claims 5-7 are indefinite for lacking the proper antecedent basis. "A" should be changed to ---The----. Also, "the cell" should be changed to ---the host cell--, for proper antecedent basis.

In claim 8, a DNA construct" lacks proper antecedent basis.

Claim Rejections - 35 USC § 112

2. Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated nucleic acids encoding the polypeptide of SEQ ID NO: 2 from cabbage, and transgenic plant and seeds comprising said nucleic acid, does not reasonably provide enablement for any nucleic acid molecule that hybridizes to SEQ ID NO: 1 under the specified conditions and still encoding a protein having the desired activity, and transgenic plants and seeds transformed with said nucleic acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to a DNA construct comprising one or more nucleic acid molecules encoding a serine protease inhibitor from cabbage having antibiosis activity, a nucleic acid molecule that hybridizes to SEQ ID NO: 1 under the defined stringent conditions and encodes a serine protease inhibitor, and transgenic plants, plant cells and seeds transformed with said DNA construct.

Applicant teaches isolation of a cDNA from a *Brassica oleracea* cDNA library prepared from young leaves by screening with cabbage protease inhibitor antibodies (Example 1; SEQ ID NO: 1, encodes SEQ ID NO: 2). Applicant teaches construct of vectors comprising the CaMV 35S promoter operably linked to the cDNA, and teaches that the encoded protein shows 30% sequence identity with soybean trypsin inhibitor-3 (Examples 3-5). Applicant also teaches transformation of tobacco with said vector and teaches that assays of trypsin and chemotrypsin inhibition activity showed higher levels of inhibitory activity by transgenic lines expressing SEQ ID NO: 2 as compared to transgenic lines expressing *Manduca sexta* anti-trypsin (Examples 7-9; Figure 4). Further, reduced growth of corn earthworm and tobacco budworm was observed when insects are fed on leaf discs from transgenic plants expressing SEQ ID NO: 2 (Example 10; Figures 5-7).

Applicant has not disclosed other nucleic acid molecules that hybridize to the disclosed sequence under the defined stringency conditions, wherein said nucleic acid molecules encode a serine proteinase inhibitor having antibiosis activity or the protease inhibition activity of SEQ ID NO: 2.

The state of the prior art teaches that not all nucleotide sequences that hybridize to each other will encode proteins of similar function, even if the hybridization conditions are relatively high stringency. For example, Lazar et al (Molecular and Cellular Biology, March 1988, Vol. 8, No. 3, pp. 1247-1257 (U)) teach a mutation of aspartic acid 47 and leucine 48 of a transforming growth factor alpha results in different biological activities (see at least the Title). Broun et al (Science, 13 November 1998, vol. 282, pp. 131-133

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(U)) teach as few as four amino acid substitutions in a protein can change the protein activity (Abstract). The proteins (mutated and original) would share high sequence identity. The Examiner notes that the nucleic acid sequences encoding said proteins disclosed by either Lazar or Broun would hybridize to each other under high stringency conditions. Therefore, it is unpredictable whether any and all nucleotide sequences that hybridize to SEQ ID NO: 1 would encode a protein with the desired functional activity.

No guidance has been provided for modifications to SEQ ID NO: 1 or a nucleotide sequence encoding SEQ ID NO: 2 that resulted a nucleic acid molecule having both the structural and functional properties as recited in the claims. Neither the instant specification nor the prior art discloses that a structural identity between two sequences would inherently imply that the two sequences have similar function. While one skilled in the art can prepare nucleic acid sequences having the claimed structural characteristics without undue experimentations, the obtention of all nucleic acid sequences having the structural and functional characteristics as recited in the claims would require extensive tests considered to be undue.

In addition, the only working example disclosed in the specification is limited to unmodified SEQ ID NO: 1. No transgenic plant or a plant part with resistance against pests as a result of expressing the nucleotide sequence of claim 2(c) has been disclosed.

Therefore, absent specific guidance for how to obtain a nucleotide sequence that hybridizes to SEQ ID NO: 1 and encoding a protein having the desired functional

activity, one skilled in the art, who is willing to practice the invention, is left with trial and error experimentations considered to be undue.

Therefore, in view of the breadth of the claims, the limited guidance and working examples, and unpredictability inherent with respect to structural identity, the claimed invention is not enabled throughout the broad scope.

See *Amgen Inc. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at 1027 (Fed. Cir. 1991) where it is taught that the disclosure of a few gene sequences did not enable claims broadly drawn to any analog thereof. In this case, the disclosure of SEQ ID NO: 1 does not enable claims broadly drawn any DNA that hybridizes thereto and transgenic plants/cells expressing said DNA for resistance against pests, absent specific further guidance.

Written Description

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a DNA construct comprising one or more nucleic acid molecules having a nucleotide sequence encoding a serine protease inhibitor from cabbage having antibiosis activity, a nucleic acid molecule that hybridizes to SEQ ID NO: 1 under the defined stringent conditions and encodes a serine protease inhibitor, and transgenic plants, plant cells and seeds transformed with said DNA construct.

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The claimed invention does not meet the current written description requirement for the following reasons. Firstly, a nucleotide sequence encoding a serine protease inhibitor from *Brassica oleracea* as claimed in claim 1 is defined by function only. The functional activity and the source of the nucleotide sequence are insufficient to provide adequate written description for the nucleotide sequence. Applicant has not described the structural, chemical or physical characteristics such as molecular weights and isoelectric points of all other serine protease inhibitors from *Brassica oleracea*, and a review of the literature does not indicate that such characteristics would be well known to a skilled artisan. Thirdly, Applicant has only described the single species of SEQ ID NO: 1. Fourthly, the state of the art as exemplified by Broadway (WO 91/09060) teaches that the efficacy of a specific proteinase inhibitor depends upon its unique structure. This implies that one has to know the structural characteristics of an inhibitor before the inhibitor can be used against specific pests. Therefore, Applicant has not adequately described the nucleotide sequences of claims 1 and 2. Consequently, Applicant fails to provide an adequate written description for expression vectors, plants, plant cells and seed comprising said sequences. Therefore, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that Applicants were in possession of the claimed invention.

See Written description Examination Guidelines published in Federal Registry/Vol. 66, No.4/Friday, January 5, 2001/Notices). See, also *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997) where it states "A

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description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus.

Remarks

SEQ ID NO: 1 and nucleotide sequences encoding SEQ ID NO: 2 are free of the prior art of record.

No claim is allowed.

Papers related to this application may be submitted to Technology Sector 1 by facsimile transmission. Papers should be faxed to Crystal Mall 1, Art Unit 1638, using fax number (703) 308-4242. All Technology Sector 1 fax machines are available to receive transmission 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Medina A. Ibrahim whose telephone number is (703) 306-5822. The Examiner can normally be reached Monday-Thursday from 8:30AM to 5:30PM and every other Friday 9:00AM to 5:00PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Amy Nelson, can be reached at (703) 306-3218.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

3/18/03

Mai



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